REMARKS

Applicants thank the examiner for her assertion that Claim 25 would be allowable if rewritten in independent form incorporating all the limitations of the base and intervening claims. This has been done. Additionally, Claim 24 has been rewritten to depend from Claim 25.

The claims have been amended to emphasize drug dilution and diffusion of the drug out of the diffuser element, which substantially distinguishes the present invention from that disclosed by Valli.

Rejections Under 35 USC 102

Claims 1-24 and 26-28 are rejected as anticipated by Valli.

The standard for an anticipation rejection I as follows:
"...for anticipation under 35 U.S.C. 102, the reference must teach every aspect of the claimed invention either explicitly or impliedly. Any feature not directly taught must be inherently present." MPEP 706.02.

Valli does not teach every aspect of the currently claimed invention.
Claim 1 of the present application, as amended, recites a drug delivery and *dilution* device that takes a drug at a first (higher) concentration and allows the drug to *diffuse* out through a "*diffuser element*" such that the drug, upon delivery, is *diluted* to a second (lower) concentration. See, for example, para. 91 of the application.

The equivalent "diffuser element" of Valli identified by the examiner (11 or 16) is, in fact, not a diffuser element at all, but merely an inflatable catheter bag with holes in it designed to inflate and deflate due to the increase and decrease of pressure of a pumped fluid. The device of Valli is used for flushing the peritoneal cavity. A liquid, presumably saline or similar, is pumped under pressure into the bag ("membrane") causing the bag to inflate. Saline is forced out of the holes into the peritoneal cavity, and "the dialyzing liquid is delivered and drawn through the catheter perforations and into and from the body cavity." (See ~~Valley~~ Valli Co. 2, lines 19-23 and col. 3 lines

15-39). Diffusion does not and cannot occur using the device of Valli, because the catheter bag uses the pressure of the liquid to pump up the bag and to force the liquid through the holes. This is not diffusion. Diffusion is the movement of small molecules from one part of a fluid to another part under the influence of the inherent kinetic energy of the molecules themselves. Diffusion tends to result in the movement of molecules away from an area of high concentration to an area of low concentration, resulting in a dilution effect. (MacMillan Dictionary of Genetics and cell Biology, 1987). The pumping action of Valli would not allow the dilution of the drug that requires diffusion of the drug from the "diffuser element" of the device into the surrounding environment.

In view of the above reasoning and amendments, it is suggested that Claim 1 is not anticipated by Valli. Claims 2-22 depend from claim 1 and are, therefore, also not anticipated by Valli.

Claim 23 is cancelled.

Claim 24 now depends from claim 25, which has been amended, as suggested by the examiner, to make it allowable.

Claims 26 and 27 recite a method for diluting an agent, and have been amended to emphasize diffusion of the agent from the device. Thus, for the same reasons as set out above, Claims 27 and 28 are not anticipated by Valli.

New Claims 29 and 30 both depend from claim 1 and therefore are not anticipated by Valli for the reasons above. Claim 29 recites the device of claim 1 wherein the diffuser element comprises a polymer (for support see para. 93). Claim 30 recites the device of claim 29 wherein the diffuser element has a Diffusion Coefficient (DC) value in the range between 4.1 x 10-6 and 3.3 x 10-5 μg/cm/sec (for support see para. 93).

Although a rejection under 35 USC 103 has *not* been given, the applicants assert that, in view of the present amendments emphasizing dilution and diffusion, and also in view of the arguments

and reasoning above, it would not have been obvious of one of skill in the art to modify the invention of Valli to make a device as claimed, that dilutes a drug from a higher to a lower concentration using diffusion from a diffuser element. If any such modification had been done, there would certainly be no reasonable expectation of success of practicing the current invention. Any drug so delivered would simply be forced from the catheter bag of Valli out into the surrounding environment at full concentration.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Attorney at (408) 864-7435.

Applicants believe that no fee is due with this paper. However, if the Commissioner determines that a fee is necessary, the Commissioner is hereby authorized to charge any additional fees associated with this communication or credit any overpayment to Deposit Account No. **50-1953. A duplicate copy of this communication is enclosed.**

If there are any questions regarding the above, the Examiner is invited to call the undersigned at 408-864-7435.

Respectfully submitted,

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Signed:

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

1. **(Once Amended)** A [local concentration management] drug delivery and dilution device comprising:

an elongate body comprising a proximal end defining an inlet, and a distal end defining an outlet, the elongate body defining a passageway extending between the proximal and distal ends; and

a diffuser element operatively associated with the elongate body so as to define a diffusion space, wherein the diffusion space is in fluid communication with the elongate body passageway;

wherein [agent] a drug at a first concentration is introduced into the elongate body inlet, moves through the elongate body passageway, out the elongate body outlet, into the diffusion space, and substantially diffuses out through the diffuser element to exit the device such that the drug, upon delivery, is diluted to a second concentration that is less than the first concentration.

2. The device of claim 1, wherein the diffuser element is the diffuser element comprising a material selected from the group consisting of a semipermiable membrane, a microporous membrane and an ion exchange membrane [whereby said diffuser element is operatively associated with the elongate body by connection to an outer wall of the elongate body].

3. The device of claim 1, wherein the elongate body and the diffuser element are operatively associated by attachment to a drug delivery device.

4. The device of claim 1, wherein the elongate body is defined by an exit orifice of a drug delivery device.

5. The device of claim 4, wherein the diffuser element is provided as a cap attached to a distal end of the drug delivery device.

6. The device of claim 1, wherein the diffusion space is defined by an outer wall of the elongate body and an inner wall of the diffuser element.

7. The device of claim 1, wherein said diffuser element envelops at least a portion of said elongate body.

8. The device of claim 1, wherein the diffuser element is microporous.

9. The device of claim 1, wherein the diffuser element is a dense membrane.

10. The device of claim 1, wherein the diffuser element is an ion-exchange membrane.

11. The device of claim 1, wherein said diffuser element distal end extends distally beyond the elongate body distal end.

12. The device of claim 1, wherein the diffuser element is ring-shaped element.

13. The device of claim 1, wherein the diffuser element is substantially impermeable to biological fluids or components of biological fluids.

14. The device of claim 1, wherein the diffuser element is selectively permeable to water.

15. The device of claim 1, wherein the device further comprises a dilutor element operatively associated with the elongate body so as to be in fluid communication with the elongate body passageway, the dilutor element comprising a selectively water permeable material to allow ingress of water for dilution of the formulation during transit through the device.

16. The device of claim 15, wherein the dilutor element comprises at least a portion of a wall of the diffuser element.

17. The device of claim 1, wherein the elongate body comprises at least two outlets.

18. The device of claim 1, wherein said elongate body defines at least two passageways.

19. The device of claim 1, wherein the elongate body passageway is adapted for delivery of agent at a low volume rate.

20. **(Once Amended)** A drug delivery system comprising:

the drug delivery and dilution device of claim 1, communicably attached to a drug-containing reservoir. [the local concentration management device according to claim 1; and a drug delivery device comprising a reservoir;

wherein the drug delivery device is attached to the provide a flow pathway from the drug delivery device reservoir, into the elongate body passageway, and out the local concentration management device.]

21. The drug delivery system of claim 20, wherein the drug delivery device is a convective drug delivery device.

22. The drug delivery system of claim 20, wherein said drug delivery device is implantable.

23. **(Cancel)** A method for delivery of an agent to a delivery site in a subject, the method comprising the steps of:

implanting at least a distal portion of a local concentration management device according to claim 1 at a delivery site in a subject; and

introducing a formulation comprising an agent into the inlet of the elongate body;

wherein the introduced agent flows through the elongate body passageway and out the local concentration management device to the delivery site in the subject.

24. **(Once Amended)** The method of clam [23] 25, wherein the formulation is introduced into the inlet at a low volume rate.

25. **(Once Amended)** A method for delivery of an agent to a delivery site in a subject, the method comprising the steps of:

implanting at least a distal portion of a local concentration management device according to claim 1 at a delivery site in a subject; and

introducing a formulation comprising an agent into the inlet of the elongate body;

wherein the introduced agent flows through the elongate body passageway and diffuses out the local concentration management device to the delivery site in the subject [The method of claim 23], wherein the elongate body passageway is at least partially filled with an agent formulation prior to said implanting.

26. **(Once Amended)** A method for diluting the concentration of an agent exiting a device, the method comprising:

implanting at least a distal portion of a local concentration management device according to claim 1 at a delivery site in a subject; and

introducing a formulation comprising an agent at a first concentration into the inlet of the elongate body;

wherein the introduced agent flows through the elongate body passageway, diffuses out the local concentration management device [and] to the delivery site in the subject, and wherein the agent in the formulation is diluted to second concentration at the delivery site, the second agent concentration being less than the first agent concentration.

27. **(Once Amended)** A method for diluting the concentration of an agent exiting a device, the method comprising:

implanting at least a distal portion of a local concentration management device according to claim 1 at a delivery site in a subject; and

introducing a formulation comprising an agent at a first concentration into the inlet of the elongate body;

wherein the introduced agent flows through the elongate body passageway, diffuses out the local concentration management device [and] to the delivery site in the subject, and wherein the agent in the formulation is diluted to second concentration prior to exit at the delivery site, the second agent concentration being less than the first agent concentration.

28. **(Cancel)** A method for dispersing a drug delivery stream, the method comprising:

implanting at least a distal portion of a local concentration management device according to claim 1 at a delivery site in a subject; and

introducing a formulation comprising an agent into the inlet of the elongate body; wherein the introduced agent flows through the elongate body passageway, out the local concentration management device and to the delivery site in the subject in a pattern that is disperse relative to a delivery pathway through the device , and wherein the agent in the formulation is diluted to second concentration at the delivery site, the second agent concentration being less than the first agent concentration.

29. **(New)** The device of claim 1 wherein the diffuser element comprises a polymer.

30. **(New)** The device of claim 29 wherein the diffuser element has a Diffusion Coefficient (DC) value in the range between 4.1 x 10-6 and 3.3 x 10-5 μg/cm/sec.